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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,425	10/07/2005	Nicola Murdoch Heron	101015-1P US	6673

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
06/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,425	HERON ET AL.	
	Examiner	Art Unit	
	TAMTHOM N. TRUONG	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment of 10-7-05 has been entered. Claims 18-21 have been cancelled. Claims 1-17 and 22-26 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating **colorectal cancer**, does not reasonably provide enablement for a method of treating hyperproliferative diseases or other cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 23 recites: "A method of treating a human suffering from a hyperproliferative disease,…" which includes the treatment for many diseases cited below:

> **[0930]** In another aspect of the invention, there is provided a compound of formula (I) or a pharmaceutically acceptable salt, ester or prodrug thereof, for use in the preparation of a medicament for the treatment of hyperproliferative diseases such as cancer and in particular colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukaemia or lymphoma. Also provided is a compound of formula (A) or a pharmaceutically acceptable salt or ester thereof for use in the preparation of a medicament for the treatment of hyperproliferative diseases such as cancer and in particular colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukaemia or lymphoma.
>
> **[0931]** In another aspect of the invention, there is provided the use of a compound of formula (I) or a pharmaceutically acceptable salt, ester or prodrug thereof, in the preparation of a medicament for the treatment of a disease where the inhibition of one or more Aurora kinase(s) is beneficial. The use of a compound of formula (A) or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a disease where the inhibition of one or more Aurora kinase(s) is beneficial is also provided. In particular it is envisaged that inhibition of Aurora-A kinase and/or Aurora-B kinase may be beneficial.
>
> **[0932]** In another aspect of the invention, there is provided the use of a compound of formula (I) or a pharmaceutically acceptable salt, ester or prodrug thereof, in the preparation of a medicament for the treatment of hyperproliferative diseases such as cancer and in particular colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukaemia or lymphoma. Also provided is the use of a compound of formula (IA) or a pharmaceutically acceptable salt or ester thereof in the preparation of a medicament for the treatment of hyperproliferative diseases such as cancer and in particular colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukaemia or lymphoma.

Thus, the scope of claim 23 is unduly broad

Claim 26 recites a method for treating specific cancers such as: colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukemia or lymphoma. Although the scope is not as broad as that of claim 23, those cancers affect different organs, and do not manifest the same way. Many of those cancers do not have cell lines tested.

The amount of direction or guidance presented: For the treatment of cancers or cell proliferation, the specification describes only two *in-vitro* assays. Both assays use only one cell line of SW620 (which is colorectal cell line). Since colorectal cells have different morphology, the inhibition on said cell line cannot be applicable for other cell types such as: breast, pancreatic, lung, prostate, renal, bladder, etc. Thus, the specification does not provide sufficient enablement for the scope of treatment recited in claims 23 and 26.

The state of the prior art: Although quinazoline compounds are known to treat cancers, it is still a challenge to treat many cancers such as small-cell lung cancer, leukemias, lymphomas, pancreatic or renal cancer. Each type of cancer metastasizes at a different rate and may or may not respond to certain drugs. Therefore, the *in-vitro* model for one cell line cannot predict the activity for other cell lines as according to **Voskoglou-Nomikos et. al.**, which discloses that not all *in-vitro* models are predictable for various types of cancers (e.g., see the abstract on page 4227). Thus, the state of the art does not support the treatment of several cancers based on the *in-vitro* model of only one cell line.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the

large Markush group of formula I. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification has not shown how a compound of formula I could treat a variety of diseases or cancers when only the cell line of SW620 has been tested.

Thus, given the unpredictable nature of the art, and the vast number of compounds claimed herein, one skilled in the art will have to carry out undue experimentation to use compounds of formula I as recited in the above claims.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-17 and 22-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of copending Application No. **10/ 559,328**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of formula I of the copending application '328 overlap with those of the instant formula I when **R^9 is hydrogen** while other variables have similar scopes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

Tamthom N. Truong
Examiner
Art Unit 1624

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6-5-08